EFFICACY EVALUATION AND TECHNICAL MANAGEMENT SECTION

ANTIMICROBIAL PROGRAM BRANCH

EFFICACY REVIEW - FORM 1

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Reviewed By: Z. Vajtauer 8/5/96

EPA Reg. No. or File Symbol: 52252-4

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EPA Petition or EUP No.: None

Product Type: Sterilant/Disinfectant

MRID No(s): None

Product Manager & Team No.: Doreen Aviado, PM-31

Product Name: Minncare Cold Sterilant

Company Name: Minntech Corp.

Submission Purpose: Response to EPA letter of 4/11/96. Rebuttal to EETMS request to delete RO membrane disinfection claims.

Product Formulation: Liquid to be diluted prior to use.

ACTIVE INGREDIENT(S)	%
Hydrogen peroxide	22.0
Peroxyacetic Acid	4.5

203.0 **LABELING**

The EPA has an ongoing Label Improvement Program to provide a mechanism to upgrade existing pesticide product labels to meet requirements previously established by regulation. In line with the Agency's Labeling Initiative, the labeling of Minncare Cold Sterilant must be brought into compliance with the labeling and/or data requirements guidelines as per the EETMS comments below in order to stamp the label with the requested amendments.

A. The following label use directions, published as DIS/TSS-15 / March 24, 1981, are to be included on the submitted label. Labeling must address these **for each recommended use**. The directions for use must include the following:

1. The major area(s) in which the product is recommended for use (e.g. homes, schools, hospitals).

2. Identification of the type of surfaces, objects, or items intended for treatment (e.g. floors, walls, bathroom fixtures, surgical instruments), in addition to any description of surface composition (e.g. stainless steel, chrome, glass, vinyl).

3. The necessity for removal of gross filth or heavy soil. In addition, instructions must be provided for thorough cleaning of surfaces prior to application of the product, unless the product has been shown to be effective in the presence of moderate amounts of representative soil. Cleaning instructions must be clearly separated from the directions for use of the product as an antimicrobial agent.

4. If the product is to be diluted, the recommended use dilution and instructions for preparing it. The units of measure (e.g. tablespoons, ounces, quarts, gallons) to be employed in diluting the product must be given, and must be understandable to the user.

5. The method(s) of application (e.g. "by sponge, mop, or spray" or "by immersion in the solution", followed by a statement such as "to wet all surfaces thoroughly").

6. The contact time necessary for effectiveness. The directions must also indicate if, and how, the product should be removed from the surfaces after the recommended exposure period.

7. The number of times or duration of time a prepared use solution may be used for immersable items (e.g. whether a fresh solution should be prepared for each batch or

for each day's use if the solution does not become diluted or soiled, or whether the solution may be re-used for a given number of batches or for a given number of days).

8. Additional instructions may be recommended by the applicant, or required by the Agency, as determined on a case-by-case basis.

(If a product label indicates that the product can be used as both a sterilant and hospital disinfectant, the registrant must submit data for both levels of efficacy at the time, in days, when diluted product shelf-life expires. This is 7 days for Minncare.)

Not all of the above items are addressed in the Directions for Sterilization, Directions for Hospital Disinfection, and Directions for Use as a Germicidal Spray. Most notably, identification of the **type of** surfaces, **objects, or items intended for treatment is missing in all three cases**.

The statement "Fresh sanitizing solution should be prepared daily or more often if the solution becomes diluted or soiled" was not included in the label as requested in the EPA letter of 4/11/96

B. The EPA letter of 4/11/96 requested that the word "disinfect" be removed and replaced with the word "sanitize" wherever it appears in the "Directions for Disinfection of RO Membranes". The Agency adopts the accepted position that the fine porous nature of RO membranes makes them impossible to disinfect by exposing them to a chemical disinfectant.

Minntech responded by submitting several publications to support the use of the word "disinfect" for RO membrane decontamination. A review of the these shows that the terms "disinfect" and "sanitize" are both used interchangeably to show a **reduction** in microbial numbers. Consider the EPA definitions of these words:

"Disinfectant" means an agent that **eliminates (not reduces)** a specific species of infectious or other undesired microorganism, but not necessarily bacterial spores, in the inanimate environment only.

A (non-food contact surface) **"sanitizer"** achieves a **reduction** of at least 99.9% (a 3-log reduction) in the number of each test microorganism over the parallel control count within 5 minutes. Examples of acceptable label claims are: "Sanitizes", "Significantly reduces", or "Reduces the number of bacteria by 99.9%."

Nothing in the submitted literature shows disinfection (elimination) of the microbes tested in RO membranes. Most studies were done in test tubes rather on RO membranes, therefore are not valid for RO membrane claims. The results are expressed in terms like "shows favorable log reduction values". These are sanitizing terms.

One study, "A Super Biocide for Disinfecting Reverse Osmosis Systems", performed by J.B.Maltais of Minntech, actually uses the terms disinfect and sanitize interchangeably (Biocide for disinfecting... recommended for cleaning and sanitizing RO membranes...). These terms are not synonymous. The 36 minute 6D value obtained for 1% Minncare in this study, unfortunately, was not done on RO membranes, but in a test tube study.

The only study most closely simulating the proposed RO membrane uses done by Asari, et al, shows a time of 2 and 3 **hours** for **disinfection** of hollow fibers.

Attachment B, "FILMEC Membranes Technical Bulletin" states that a 0.25% solution of Minncare in **"A soak time of 2 hours would be expected to kill more than 90% of the bacteria, whereas a 12 hour soak-time would achieve a 99% kill."**

These are still sanitizing claims and do not even meet the EPA criteria for non-food contact surface sanitization, which is a reduction of at least 99.9% **(a 3-log reduction)** in the number of each test microorganism over the parallel control count **within 5 minutes.**

In summary, the presented materials do not show disinfection of RO membranes, but rather a sanitization capability by Minncare.

C. The first paragraph under "Directions for disinfection of RO Membranes", referred to as "Reverse Osmosis Application Note" in the previous draft label, must be upgraded to conform to the original language required by the Agency for RO membrane use, which is as follows:

SANITIZATION OF REVERSE OSMOSIS MEMBRANES:

"This product has been shown to be an effective disinfectant when tested by AOAC and EPA methods. This product may not totally eliminate all vegetative microorganisms in reverse osmosis membranes and their associated piping systems due to their construction and/or assembly, but can be relied upon to reduce the number of microorganisms to acceptable levels when used as directed."

The above note is necessary because without it, it is false and misleading to claim that RO membranes can be disinfected. The publications supplied with the current submission do, in fact, support this position (of sanitization, not disinfection).

D. Since the submitted publications deal with RO membranes in kidney dialysis machines, the RO membrane Directions must include a clear statement that **"This product is not registered for use on kidney dialysis membranes"**. This is necessary so as not to mislead the users into using this product for uses that need FDA clearance.

E. Additional support for the fact that disinfection is not an appropriate term is seen by the Agency's position on Circulate-In-Place (CIP) Applications. Label claims for CIP applications as "germicidal" or "disinfecting" are not acceptable because these methods have not been shown to be an effective means of disinfecting surfaces in these systems. Representations for CIP applications to sanitize the surfaces of the systems are acceptable.